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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,360	01/05/2005	Julie Kay Bush	X-14884	5540
25885	7590	08/16/2007	EXAMINER	
ELI LILLY & COMPANY PATENT DIVISION P.O. BOX 6288 INDIANAPOLIS, IN 46206-6288			QAZI, SABIHA NAIM	
ART UNIT		PAPER NUMBER		
1616				
NOTIFICATION DATE		DELIVERY MODE		
08/16/2007		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/520,360	BUSH ET AL.
	Examiner Sabiha Qazi	Art Unit 1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 7/11/07.  
 2a) This action is FINAL.                            2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*; 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 2 and 15 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 2 and 15 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____	5) <input type="checkbox"/> Notice of Informal Patent Application
	6) <input type="checkbox"/> Other: _____

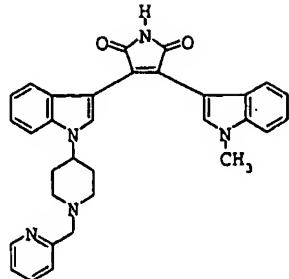
**Non-Final Office Action**

Claims 2 and 15 are pending. Amendments are entered.

**Summary of this Office Action dated August 11, 2007**

1. 35 USC § 102 (b) Rejections
2. 35 USC § 103(a) --Rejection
3. Response to Remarks
4. Communication

Upon further review and consideration finality of the rejection is withdrawn. New rejections are being made.



**35 USC § 102(b)-- Rejection**

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 2 and 15 rejected under U.S.C. 102(b) as being anticipated by TEICHER et al<sup>1</sup>. See the entire document, especially lines 1-5 on page 9, lines 1-10 on page 7, lines 13-32, page 8, lines 27-31 on page 11, lines 20-30 on page 14, all examples, and claims especially claims 1, 3-7, 13.

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<sup>1</sup> BEVERLY TEICHER et al; World Intellectual Property Organization Publication Number WO 02/02094 A2, published January 10, 2002.

TEICHER et al discloses the present compound, FB, in crystalline form and its salts, exemplified compound is dihydrochloride salts. The reference discloses the compound, compositions, and methods of treating neoplasm, and the combination with other antineoplastic agents.

Compound of formula 1 on page 7 is 3-[l- (1-(pyridin-2 methyl)piperidin-4-yl)-indol-3-yl]-4-(1 -methyhdol-3-yl)- 1H-pyrrole-2,5-dione or a pharmaceutically acceptable salt or solvate thereof (see lines 1-10 on page 7). Monohydrochloride salt of this compound is presently claimed.

It further discloses, "Because it contains a basic moiety, the compound of Formula I can also exist as pharmaceutically acceptable acid addition salts. Acids commonly employed to form such salts include inorganic acids such as hydrochloric, (lines 13-32, page 8).

Reference further discloses that the pharmaceutically acceptable salts of the compound of Formula I can also exist as various solvates, such as with water, methanol, ethanol, dimethylformamide, ethyl acetate and the like. Mixtures of such solvates can also be prepared. The source of such solvate can be from the solvent of crystallization, inherent in the solvent of preparation **or crystallization**, or adventitious to such solvent. (see lines 1-5 in column 9).

In claim 2 the Applicant has cited the X-ray diffractions of their crystalline compound. However, since TEICHER et al discloses the crystalline forms of this compound and since the compound of prior art exists in crystalline form has the same

utility and since no distinction has been made, claim 2 is considered anticipated by the prior art. The pharmaceutical composition will be the same as the prior art because the compound is the same.

Since there is no showing, teaching or comparative data that the prior art hydrochloride is not the same as presently claimed, the claims of the present invention is anticipated by the reference.

**35 USC § 102 (b) 2<sup>nd</sup> Rejection**

Claims 2 and 15 are rejected under 35 U.S.C. 102 (b) as being anticipated by HEATH et al<sup>2</sup>. See the entire document, especially Example 49 in col. 45 and 46, Examples 45 and 46 in col. 43 and 44, Formulas II and III in col. 3 and 4.

HEATH et al discloses the present compound, compositions, and methods of use. The reference discloses pharmaceutically acceptable salts such as hydrochloric salts.<sup>3</sup> The reference also discloses that the compounds are potent, beta-1 and beta-2 isozyme selective PKC inhibitors.

In claim 2 the Applicants have cited the X-ray diffractions of their crystalline compound. HEATH et al discloses the same compound. The pharmaceutical composition is also discloses by the reference.

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<sup>2</sup> WILLIAM F. HEATH, JR. et al; United States Patent No. 5,545,636, published August 13 1996. See the entire document, especially Example 49 in col. 45 and 46, Examples 45 and 46 in col. 43 and 44, Formulas II and III in col. 3 and 4, examples, abstract, and claims.

<sup>3</sup> See lines 35-67 in col. 10.

The instant invention is anticipated by the prior art because applicant provide no evidence that the X-ray diffraction of their compound is different is different from prior art compound.

**Claim Rejections - 35 USC § 102**

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 2 and 15 rejected under 35 U.S.C. 102(e) as being anticipated by HEATH et al. (for the same reasons as cited above).

The applied reference has a common assignee with the instant application.

Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

**35 USC § 103(a) --- First Rejection**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 15 are rejected under 35 U.S.C. 103(a) as being obvious over TEICHER et al<sup>4</sup>.

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<sup>4</sup> BEVERLY TEICHER et al; World Intellectual Property Organization Publication Number WO 02/02094 A2, published January 10, 2002. See the entire document, especially lines 6-10 on page 9, lines 1-10 on page 7, lines 27-30 on page 11, all of pages 12-20, examples, and claims.

Compound of formula 1 on page 7 is 3-[l- (1-(pyridin-2 methyl)piperidin-4-yl)-indol-3-yl]-4-(1 -methyhdol-3-yl)- 1H-pyrrole-2,5-dione or a pharmaceutically acceptable salt or solvate thereof (see lines 1-10 on page 7). Monohydrochloride salt of this compound is presently claimed.

It further teaches, "Because it contains a basic moiety, the compound of Formula I can also exist as pharmaceutically acceptable acid addition salts. Acids commonly employed to form such salts include inorganic acids such as hydrochloric acid (lines 13-32, page 8).

Reference further teaches that the pharmaceutically acceptable salts of the compound of Formula I can also exist as various solvates, such as with water, methanol, ethanol, dimethylformamide, ethyl acetate and the like. Mixtures of such solvates can also be prepared. The source of such solvate can be from the solvent of crystallization, inherent in the solvent of preparation **or crystallization**, or adventitious to such solvent. (see lines 1-5 in column 9).

TEICHER et al teaches the present compound, FB, and its salts, especially dihydrochloride salts. The reference teaches the compound, compositions, and methods of treating neoplasm, and the combination with other antineoplastic agents.

Instant invention differs from the reference in claiming a crystalline compound, and methods of treating various diseases.

In claims 2 and 3, the Applicants have cited the X-ray diffractions of their crystalline compound. However, it would have been obvious to one skilled in the art at

the time of invention to prepare the crystalline pharmaceutically acceptable salts such as hydrochloride salts because the prior art teaches TEICHER et al teaches the crystalline forms of this compound. The pharmaceutical composition and the method of using will be the same as the prior art because the compound is the same.

Applicant must provide additional evidence to establish why their compound should be considered non-obvious, in absence of additional evidence to contrary, applicant's evidence must be deemed insufficient.

In absence of any criticality and/or unexpected results, the instant invention is considered *prima facie* obvious over the cited prior art.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

### **35 USC § 103(a) --- Second Rejection**

Claims 2 and 15 are rejected under 35 U.S.C. 103(a) as being obvious over HEATH et al<sup>5</sup>.

HEATH et al teaches the present compound, compositions, and methods of use. This compound is a protein kinase inhibitor. The reference teaches pharmaceutically

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<sup>5</sup> WILLIAM F. HEATH, JR. et al; United States Patent No. 5,545,636, published August 13 1996. See the entire document, especially Example 49 in col. 45 and 46, Examples 45 and 46 in col. 43 and 44, Formulas II and II in col. 3 and 4, examples, abstract, and claims.

acceptable salts such as hydrochloric salts.<sup>6</sup> The reference also teaches the compounds are potent, beta-1 and beta-2 isozyme selective PKC inhibitors.

Instant invention differs from the reference in having a narrower scope than the prior art.

In claims 2 the Applicants have cited the X-ray diffractions of their crystalline compound. However, since the compound are potent, beta-1 and beta-2 isozyme selective PKC inhibitors, one skilled in the art at the time of invention would have been motivated to prepare the crystalline acid addition salts pharmaceutically acceptable salts such as hydrochloride salts because HEATH et al teaches the crystalline forms of this compound. The pharmaceutical composition and the method of using will be the same as the prior art because the compound is the same.

X-ray diffraction data presented in claim 2 is not a comparative data. Applicant has provided no data for distinguishing their invention with the prior art. Due to the teachings of the prior art presently claimed invention is considered *prima facie* obvious to one skilled in the art. Applicant must provide additional evidence to establish why their compound should be considered non-obvious, in absence of additional evidence to contrary, applicant's evidence must be deemed insufficient.

In absence of any criticality and/or unexpected results, the instant invention is considered *prima facie* obvious over the cited prior art.

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<sup>6</sup> See lines 35-67 in col. 10.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

**Response to Remarks**

Applicant request to withdrawn the finality has been acknowledged.

Examiner notes, that Applicants are silent over the rejection over TEICHER et al reference.

**Communication**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi, Ph.D. whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter, Ph.D. can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



SABIHA QAZI, PH.D  
PRIMARY EXAMINER